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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/943,458	Weller
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 24, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11 and 15-27* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11 and 15-27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *0403*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claim 1 has been amended and claims 12-14 have been cancelled.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-5, 10, 15, and 18-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Summerton et al. (U.S. Patent 5,034,506) (July 23, 1991).

Summerton et al teach a method of analyzing a population of oligomeric analyte molecules, wherein the molecules are composed of linked subunits of which at least 50% are uncharged, and are able to hybridize via Watson-Crick base pairing with a specific probe molecule which is a nucleic acid or charged nucleic acid analog (Abstract and Figures 1-2), the method comprising:

(a) applying to a charge-bearing separation medium a mixture of (I) the population of analyte molecules and (ii) the probe molecule, under conditions such that complementary or near-complementary regions of the probe and at least one such analyte molecule are stably hybridized, thereby forming a mixture of species selected from probe-analyte duplex, single stranded analyte,

single stranded probe, and combinations thereof (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49), and

(b) inherently separating the species within the medium (Example 19, Column 32, lines 48-59 and Column 12, line 15 to column 13, line 48 and Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49).

Summerton et al teach a method, wherein the nucleotide sequence of each analyte molecule is selected from a selected sequence (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49).

Summerton et al inherently teach a method, wherein the deletion, insertion or mutation variants contain at most one such deletion, insertion or mutation per 8 nucleotides of the selected sequence (Column 13, lines 46-48 and Examples 18-21).

Summerton et al inherently teach a method, wherein the probe has a length and a sequence such that its duplexes with different analyte molecules differ with respect to the presence, length or position of an unhybridized portion of the nucleic acid (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49 and Figure 16).

Summerton et al teach a method, wherein the probe includes a sequence complementary to the selected sequence (Example 19, Column 33, lines 22-3[illegible] , umn 34, lines 22-49, and Example 21, Column 35, lines 41-49 and Figure 16).

Summerton et al inherently teach a method, wherein variations in sequence or length among the analyte molecule occur within a given subregion of the selected sequence, and the

probe is effective to stably hybridize to the subregion under the conditions of the analysis (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49 and Figure 16).

Summerton et al inherently teach a method, wherein the subregion is at or near a terminus of the analyte molecule (Figure 16).

Summerton et al inherently teach a method, wherein the terminus is the 5' or 3' terminus of the analyte molecule and the probe comprises a labeling moiety at its 5' or 3' terminus (Column 14, lines 55-68).

Summerton et al inherently teach a method, wherein the charge bearing support is an ion exchange medium, and the separating step comprises passing an eluant through the medium (Column 12, line 65 to column 13, line 6).

Summerton et al teach a method, wherein all of the subunits of the morpholino oligomers analyte molecules are uncharged (Abstract, Figures 1-3 and Column 3, line 1 to column 6, line 55).

Summerton et al teach a method, wherein the morpholino oligomers have intersubunit linkages selected from the group consisting of phosphoramidate and phosphordiamidate (Abstract, Figures 1-3 and Column 3, line 1 to column 6, line 55).

Summerton et al teach a method, wherein the probe is selected from DNA (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49).

Summerton et al teach a method, further comprising the step of isolating, detecting and quantitating a duplex of the labeled probe with at least one target analyte molecule in the population (Example 19, Column 33, lines 22-39, Example 20, Column 34, lines 22-49, and Example 21, Column 35, lines 41-49 and Column 15, lines 34-50).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Summerton et al. (U.S. Patent 5,034,506) (July 23, 1991).

Summerton et al teach the method of claims 1-5, 10, 12-13, 15, and 18-27 as described above.

Summerton et al do not teach the method wherein the probe has a length equal to or no more than 25% greater than the selected sequence.

However, it is *prima facie* obvious that selection of the specific probe length of a nucleic acid hybridization reaction represent routine optimization with regard to sequence, length and compositions of the DNA sequences being screened as well as the size and sequence of the probe molecule and the requirement of screening speed which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific probe length of a nucleic acid hybridization reaction performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

6. Claims 7-9, and 11 are rejected under 35 U.S.C. 103(a) over Summerton et al. (U.S. Patent 5,034,506) (July 23, 1991) in view of Connolly et al. (U.S. Patent 6,342,370 B1) (January 29, 2002).

Summerton et al. teach method of claims 1-6, 10, 12-13, 15, and 18-27 as described above.

Summerton et al. do not teach the method, wherein the probes comprise deletion variant sequences.

Connolly et al. teach the method, wherein the probes comprise deletion variant sequences (Column 4, line 42 to column 5, line 21).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the probes comprise deletion variant sequences of Connolly et al. in the method of Summerton et al., since Connolly et al. state, "There is provided a method of diagnosing a disease or a susceptibility to a disease related to a mutation in the nucleic acid sequence and the proteins encoded by such nucleic acid sequence (Column 2, lines 46-50) ." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the probes comprise deletion variant sequences of Connolly et al. in the method of Summerton et al., in order to improve the process for analyzing a population of oligomeric analyte molecules and also in order to achieve the express advantages, as noted by Connolly et al., of an invention which provides a method of diagnosing a disease or a susceptibility to a disease related to a mutation in the nucleic acid sequence and the proteins encoded by such nucleic acid sequence.

7. Claim 16 is rejected under 35 U.S.C. 103(a) over Summerton et al. (U.S. Patent 5,034,506) (July 23, 1991) in view of Gilmanshin et al. (U.S. Patent 6,263,286 B1) (July 17, 2001).

Summerton et al. teach the method of claims 1-6, 10, 12-13, 15, and 18-27 as described above.

Summerton et al. do not teach the method, wherein the labeling moiety is a fluorescent label.

Gilmanshin et al. teach the method, wherein the labeling moiety is a fluorescent label. (Column 20, line 7 to column 26, line 43).

Summerton et al. do not teach the method, wherein the charge bearing support is an electrophoresis medium, and the separating of step (b) comprises applying an electric field between opposing boundaries of the medium.

Gilmanshin et al. teach the method, wherein the charge bearing support is an electrophoresis medium, and the separating of step (b) comprises applying an electric field between opposing boundaries of the medium (Column 19, lines 12-24).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the labeling moiety is a fluorescent label and wherein the charge bearing support is an electrophoresis medium, and the separating of step (b) comprises applying an electric field between opposing boundaries of the medium of Gilmanshin et al. in the method of Summerton et al., since Gilmanshin et al. state, "The

opportunity for multiple use of the same sample in the methods of the invention either to enhance statistics or for complementary analyses allows the use of small amounts of sample (potentially down to the single molecule level) for elaborate analyses (Column 19, lines 36-41)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the labeling moiety is a fluorescent label and wherein the charge bearing support is an electrophoresis medium, and the separating of step (b) comprises applying an electric field between opposing boundaries of the medium of Gilmanshin et al. in the method of Summerton et al, in order to improve the process for analyzing a population of oligomeric analyte molecules and also in order to achieve the express advantages, as noted by Gilmanshin et al., of an invention which provides the opportunity for multiple use of the same sample to enhance statistics or for complementary analyses which allows the use of small amounts of sample (potentially down to the single molecule level) for elaborate analyses.

8. Claim 17 is rejected under 35 U.S.C. 103(a) over Summerton et al. (U.S. Patent 5,034,506) (July 23, 1991) in view of Gilmanshin et al. (U.S. Patent 6,263,286 B1) (July 17, 2001) further in view of Hearn et al. (U.S. Patent 4,279,724) (July 21, 1981).

Summerton et al. in view of Gilmanshin et al. teach method of claims 1-6, 10, 12-16 and 18-27 as described above.

Summerton et al. in view of Gilmanshin et al. do not teach the method, wherein the medium includes a superimposed pH gradient.

Hearn et al. teach the method, wherein the medium includes a superimposed pH gradient (Abstract, Figure 14, and Example 8).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the medium includes a superimposed pH gradient of Hearn et al. in the method of Summerton et al. in view of Gilmanshin et al., since Hearn et al. state, "The method described in this invention permits large sample loadings of mixture of proteins and other biological substances and the focused zones can be easily recovered in high yield without significant loss of biological activity (Column 1, lines 49-53)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the medium includes a superimposed pH gradient of Hearn et al. in the method of Summerton et al. in view of Gilmanshin et al. in order to improve the process for analyzing a population of oligomeric analyte molecules and also in order to achieve the express advantages, as noted by Hearn et al., of an invention which permits large sample loadings of mixture of proteins and other biological substances and the focused zones can be easily recovered in high yield without significant loss of biological activity.

Response to Amendment

9. In response to amendment, 112 (second paragraph) rejections are withdrawn. However, 102(b) and 103(a) rejections are hereby properly maintained.

Response to Arguments

10. Applicant's arguments filed on April 24, 2003 have been fully considered but they are not persuasive.

Applicant argues that (Page 8, second to fifth paragraph) 102 (b) rejection should be withdrawn because Summerton reference (U.S. Patent 5,034,506) does not teach the steps (a) and (b) of claim 1. This argument is not persuasive. Summerton clearly teaches step (a), which is applying a population of different analyte molecules and the probe molecules (labelled morpholino-based oligonucleotide analogs in this case)to a charge-bearing separation medium (Column 17, line 42 to Column 18, line 47 and Figures 8A-B and Column 31, line 58 to Column 32, line 68). Summerton also clearly teaches step (b), which is separating, within a charged medium, probe-analyte duplexes from each other (Examples 20-21).

Applicant also argues (Page 9, last line to page 10, fifth paragraph) that 103 (a) rejections should be withdrawn because there is no suggestion in the combinatory references to combine the invention of Summerton with other references. This argument is not persuasive, especially in the presence of strong motivation provided by Connolly et al. since Connolly et al. state, "There is provided a method of diagnosing a disease or a susceptibility to a disease related to a mutation in the nucleic acid sequence and the proteins encoded by such nucleic acid sequence (Column 2, lines 46-50) ." The same reasonings are applicable to other combinatory references as well.

In view of the response to arguments, all previous 102(b) and 103(a) rejections are hereby properly maintained.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

May 26, 2003

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